CLAIMS

We claim:

1. A purified leptin peptide, and fragment, homologs, analogs and derivatives thereof, wherein the peptide has the following characteristics:

   (a) it is a substantially homogenous preparation; and

   (b) it has at least 70% homology to any one of the sequences set forth in SEQ ID NOS: 2-16 and 18, wherein

   (c) the leptin peptide modulates body mass.

2. The leptin peptide of claim 1, wherein the leptin peptide does not bind to the leptin receptor.

3. The leptin peptide of claim 1, wherein the leptin peptide can cross the blood brain barrier.

4. A leptin peptide having the amino acid sequence Xaa_n-Ser-Cys-Xaa_1-Leu-Pro-Xaa_2-Xaa_3-Xaa_n, wherein:

   (a) Xaa_n may be 0 or a contiguous stretch of peptide residues derived from SEQ ID NOS: 1 or 17; and

   (b) Xaa_1, Xaa_2 and Xaa_3 may be any amino acid substitution.

5. The leptin peptide of claim 4, wherein Xaa_1, Xaa_2 and Xaa_3 may be any conservative amino acid substitution.

6. The leptin peptide of claim 4, wherein:

   (a) Xaa_1 may be selected from the group consisting of His or Ser;

   (b) Xaa_2 may be selected from the group consisting of Trp or Gln; and

   (c) Xaa_3 may be selected from the group consisting of Ala or Thr.

7. The peptide of claim 1, wherein the peptide is an OB-3 peptide selected from amino acid residues ^{116}Ser-Cys-Ser-Leu-Pro-Gln-Thr^{122} of mouse leptin protein [SEQ ID NO:2] or ^{116}Ser-Cys-His-Leu-Pro-Trp-Ala^{122} of human leptin protein [SEQ ID NO:18], and fragments, derivative, homologs and analogs thereof.

8. The peptide of claim 1, wherein the peptide is a mammalian peptide.

9. The peptide of claim 1, wherein the peptide is a murine peptide.

10. The peptide of claim 1, wherein the peptide is a human peptide.

11. The peptide of claim 1, wherein the peptide is a synthetic peptide.

12. A peptide comprising amino acid residues of the leptin protein of any one of SEQ ID NOS:1 and 17, selected from the group consisting of:

(i) amino acid residues 21-35 [SEQ ID NO:3];

(ii) amino acid residues 31-45 [SEQ ID NO:4];

(iii) amino acid residues 41-55 [SEQ ID NO:5];

(iv) amino acid residues 51-65 [SEQ ID NO:6];

(v) amino acid residues 61-75 [SEQ ID NO:7];

(vi) amino acid residues 71-85 [SEQ ID NO:8];

(vii) amino acid residues 81-95 [SEQ ID NO:9];

(viii) amino acid residues 91-105 [SEQ ID NO:10];

(ix) mouse amino acid residues 116-122 [SEQ ID NO:2];

(x) human amino acid residues 116-122 [SEQ ID NO:18]; and

and fragments, derivatives, homologs and analogs thereof.

13. The leptin peptide of claim 1, wherein said homology to any one of the sequences set forth in SEQ ID NOS:2-16 and 18 is greater than 85%.

14. The leptin peptide of claim 13, wherein the homology is greater than 95%.

15. The leptin peptide of claim 7, and variants thereof, with conservative amino acid substitutions.

16. The leptin peptide of claim 14, and variants thereof, with conservative amino acid substitutions.

17. The leptin peptide of claim 15, wherein the conservative amino acid substitutions represent a single amino acid substitution in the mature sequence, wherein the both the substituted and replacement amino acids are non-cyclic.

18. A pharmaceutical composition comprising any one of the leptin peptides of claims 1-17, and a pharmaceutically acceptable carrier.

19. A method for treating a pathophysiology relating to homeostasis of body mass, comprising administering to a subject a therapeutically effective amount of a pharmaceutical composition comprising a leptin peptide, or fragments, homologs, analogs and derivatives thereof, wherein the leptin peptide has the following characteristics:

(a) it is a substantially homogenous preparation; and

(b) it has at least 70% homology to any one of the sequences set forth in SEQ ID NOS: 2-16 and 18 wherein

(c) the leptin peptide modulates body mass.

20. A method for preventing a pathophysiology relating to homeostasis of body mass, comprising administering to a subject a therapeutically effective amount of a pharmaceutical composition comprising a leptin peptide, or fragments, homologs, analogs and derivatives thereof, wherein the leptin peptide has the following characteristics:

(a) it is a substantially homogenous preparation; and

(b) it has at least 70% homology to any one of the sequences set forth in SEQ ID NOS: 2-16 and 18, wherein

(c) the leptin peptide modulates body mass.

21. The method of any one of claims 19 or 20, wherein the pathophysiology is obesity.

22. The method of any one of claims 19 or 20, wherein the pathophysiology is a pathophysiology related to obesity comprising any one of hyperglycemia, hyperinsulinemia, hyperphagia, thyroid dysfunction, infertility, Type II diabetes mellitus and non-insulin-dependent diabetes mellitus (NIDDM).

23. The method of any one of claims 19 or 20, wherein the pathophysiology is anorexia.

24. The method of any one of claims 19 or 20, wherein the pathophysiology is any one or more of hematopoiesis dysfunction and tumor suppression.

25. The method of any one of claims 19 or 20, wherein the step of administering to a subject comprises intraperitoneal administration.

26. An isolated nucleic acid comprising a nucleotide sequence encoding any one of the leptin related peptides of SEQ ID NOS: 2-16 and 18, and fragments, derivative, homologs and analogs thereof of those peptides.

27. A vector comprising the nucleic acid of claim 26.

28. A cultured cell that produces a leptin peptide according to any one of claims 1-17.

29. The cell of claim 28, wherein the cell is selected from the group consisting of bacteria, yeast, mammalian cells, plant cells and insect cells.

30. A method for preparing a leptin peptide comprising:

(a) culturing a cell containing a nucleic acid according to claim 26 under conditions that provide for expression of the peptide of the invention; and

(b) recovering the expressed peptide.

31. The peptide of any one of claims 1-17, wherein the peptide contains at least one D-amino acid substitution.

32. The peptide of any one of claims 1-17, wherein the peptide contains at least one variant amino acid substitution selected from the group comprising C_a-methylamino acids, N_a-methylamino acids and α,β-unsaturated amino acids.

33. The peptide of any one of claims 1-17, wherein the peptide is cyclized.

34. A linear coupled peptide having at least two peptides derived from discontinuous regions of the full length leptin protein of SEQ ID NOS:1 or 17, wherein at least one of the coupled peptides is a peptide according to any one of claims 1-17.

35. A pharmaceutical composition comprising a nucleic acid of claim 26, wherein the nucleic acid encodes a leptin peptide, and a pharmaceutically acceptable carrier.

36. An antibody, and fragments, derivatives, homologs and analogs thereof, specific for the peptide of any one of claims 1-17.

37. An antibody of claim 36 labeled with a detectable label.

38. An antibody of claim 36, wherein said antibody is generated using any one of the peptides of SEQ ID NOS:2-16 and 18, and fragments, derivatives, homologs, and analogs of said peptides.

39. A kit comprising in one or more containers a leptin peptide according to any one of claims 1-17, a nucleic acid according to claim 26, or an antibody that recognizes a leptin peptide according to any one of claims 36-38.

40. A recombinant non-human animal containing a nucleic acid, wherein the nucleic is an isolated nucleic acid comprising a nucleotide sequence encoding any one of the leptin related peptides of SEQ ID NOS: 2-16 and 18, and fragments, derivative, homologs and analogs thereof of those peptides.

41. A method of identifying a drug useful in a weight loss diet regimen comprising:

(a) administering doses of any one or more of the leptin peptides of SEQ ID NO:2-16 and 18 to a test animal and compare to a placebo control animal over a prescribed time period; and

(b) determining the change in weight of the test animal compared to the control during the prescribed time period;

wherein a peptide that causes the test animal to lose weight relative to the control animal is selected as a drug that is useful in a weight loss diet regimen.

42. A method of identifying a modulator and/or potential modulator of body mass homeostasis *in situ* comprising:

(a) contacting a cell with the presence or absence of a peptide comprising any one or more of the peptides depicted in SEQ ID NOS: 1-16 and 18;

(b) determining the level of desired effect in cells so contacted compared to cells not so contacted; wherein

when an increase or decrease in desired effect is determined in the presence of the peptide relative to in the absence of the peptide, the peptide is identified as a potential modulator of body mass homeostasis.